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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,561	04/28/2006	Satoru Oi	66540(46590)	3635

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EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/577,561	OI ET AL.	
	Examiner	Art Unit	
	BINTA M. ROBINSON	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,6,7,12 and 22-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,6,7,12,22,23,25,27,30-33,36 and 37* is/are rejected.

7)☒ Claim(s) *24, 26, 28, 29, 38-42* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/1/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

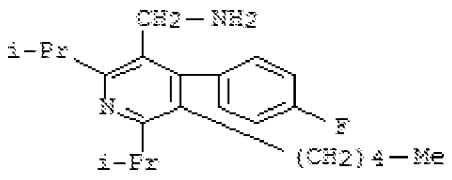
The 102 (b) rejection over Schoen et. al., the 102 (b) and 103 (a) rejections over Hcaplus 1997:9205, and the 103 (a) rejection over Schoen et. al. beginning on page 4 of the outstanding office action are withdrawn in light of applicant's amendments and remarks filed 3/20/09. The 103 (a) rejection over Hcaplus 2001:278024 in view of Patani are modified below. Claims 6, 7, 12, will be rejoined for examination although withdrawn by applicant, since they were present in the elected group I invention. New claims 34-35 are withdrawn from examination as being drawn to a non-elected invention.

(modified rejections)

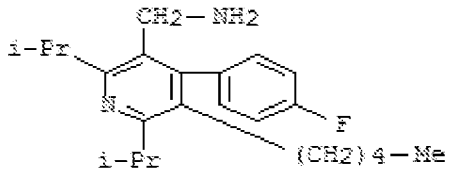
1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 6, 7, 12, 22, 23, 25, 27, 30, 31-33, 36-37, are rejected under 35 U.S.C. 103(a) as being unpatentable over Hcaplus 2001:278024 in view of Patani et. al .

3. Hcaplus 2001:278024 teaches the compound, 

. The difference between the prior art compound and the instantly claimed compounds is the teaching of an X moiety which is methyl rather than amino in the instant claim. Patani et. al. teaches that methyl and amino. At page 3152, Patani et. al. teaches that

amino and methyl are bioisosteric replacements for hydrogen. Bioisosteres are able to elicit similar biological activity or enhanced pharmacological properties to the compounds that they are replacing due to similar chemical characteristics to these compounds. It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare a bioisostere which like the instant compound, is a bioisosteric compound replacement for the compound when X is equal to hydrogen. For instance, see the compound, 

, where a disclosed species is exemplified. Accordingly, the compounds and compositions are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds and compositions over those of the prior art compounds and compositions.

(new rejections)

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 3, 6, 7, 12, 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 3, 6, 7, 12, 27 recite the limitation "The compound of claim 1" in line 1. There is insufficient antecedent basis for this limitation in the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 31 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the compounds of formula I and Ia for treating obesity or impaired glucose tolerance is not enabled for preventing any of the diseases claimed, or treating diabetes, or diabetic complications. The specification does not enable any skilled pharmacologist or physician to use the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized below.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1)the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art 6) the amount of direction provided by the inventor 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The main issues are the correlation between clinical efficacy for prevention and treatment of diabetes, diabetic complications, impaired glucose tolerance or obesity and Applicants' *dipeptidyl peptidase IV inhibitory* assay.

a) Determining if any particular claimed compound would treat or prevent any particular disease would require synthesis of the compound, formulation into a suitable dosage form, and testing these compounds in an assay known to be correlated to clinical efficacy of such treatment or prevention of the diseases claimed. This is a large quantity of experimentation given the large number of non-obvious compounds claimed. b) The direction concerning treating and preventing the diseases claimed diseases are found at pages 419 through 421. Dipeptidyl peptidase IV inhibitory assays are disclosed but it is unclear if this assay is correlated to the prevention and treatment of the claimed diseases. c) There is no working example of treatment or prevention of the claimed diseases in any mammal or other animal. d) The nature of the invention is clinical treatment of diabetes, diabetic complications, impaired glucose tolerance or obesity with the claimed compounds, which involves physiological activity. e) The state of the clinical arts in is that DPP-IV inhibitors have potential side effects with chronic use and will require ongoing scrutiny of the risk-benefit ratio for this therapy. See Abstract of Druker, page 2929. The large number of potential bioactive peptide substrates pose important questions regarding unanticipated side effects associated with the long-term use of DPP-IV inhibitors. See page 2935 of Drucker.

f) The artisan using Applicants invention would be a medicinal chemist with a PhD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain). h) The scope of the claims involves all of the thousands of compounds of claim 1 as well as the hundred of diseases embraced by the phrases "diabetic complications", "impaired glucose tolerance", "diabetes" or "obesity". Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Claims 24, 26, 28, 38 are objected to because they are based on a rejected claim.

(Response to Applicant's Remarks)

The applicant's assert that the limitation of the R4 group to an amino group and the X to a group other than hydrogen in the instant compounds overcomes the 103 (a) rejection over Hcaplus 2001:278024 in view of Patani. However, this is not so because the prior art compounds along with the instant compounds are both bioisosteric replacements of the instant compounds when X could be hydrogen, and are thus, expected to exhibit similar biological and chemical properties and pharmacological effects and therefore, the instant compounds are non-obvious over the prior art compounds.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Janet Andres can be reached on 571-272-0670.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703305-3592, and (703305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

/Binta M Robinson/
Examiner, Art Unit 1625

/Janet L. Andres/
Supervisory Patent Examiner, Art Unit 1625